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10/810,358	03/26/2004	Ker-Sang Chen	9188R&	1244

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EXAMINER	
SHAFER, SHULAMITH H	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/810,358	CHEN ET AL.	
	Examiner	Art Unit	
	SHULAMITH H. SHAFER	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2000*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *13-15 and 24-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 16-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/28/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, And/Or Claims:

The amendment received 28 November 2007 has been entered. Claims 1-45 are pending in the instant application. Claims 13-15 and 24-45 are withdrawn as being drawn to a non-elected invention. Claims 2-5, 9-12, and 14-22 have been amended and the amendment made of record.

Claims 1-12, and 16-23 are under consideration.

Withdrawn Objections/Rejections

Information Disclosure Statement:

The Information Disclosure statements (IDS) submitted on the 28 November 2007 has been considered. The signed copy is attached. The supplemental IDS overcomes the objection to the IDS filed 22 February 2007; the objection is therefore withdrawn.

Claims:

The objection to Claims 18 and because of the grammatical errors in the claims is withdrawn in view of Applicant's amendment to the claims.

Claim Interpretation:

It is noted that Claim 22 is written so as to invoke 112, 6th paragraph which states:

An element in a claim for a combination may be expressed as a means or step for performing a specified function without the recital of structure, material, or acts in support thereof, and such claim shall be construed to cover the corresponding structure, material, or acts described in the specification and equivalents thereof.

Claims 22 and 23 will be evaluated under 35 U.S.C. 112, sixth paragraph.

Maintained/New Grounds for Rejections

35 U.S.C. § 112, Second Paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of Claims 1-12, and 16-23 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for reasons of record and for reasons set forth below.

Claim 1, the independent claim of the instant invention is an incomplete method claim. Claims are incomplete for omitting essential steps. While all of the technical details of a method need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is to be practiced.

The method steps recite measuring the level of at least one anti-inflammatory cytokine and at least one pro-inflammatory cytokine in a biological sample before and after treatment. The method taught in the working example comprises drawing venous blood from each subject before and after oral feeding with a probiotic preparation (treatment). PBMCs isolated from blood of patients were incubated *in vitro* with a probiotic preparation. The quantity of cytokines in supernatant of culture media was measured. Therefore, cytokines were not measured in a biological sample from a mammalian subject, as required by the claim; rather, cytokines secreted by cells stimulated *in vitro* were measured in the exemplary method disclosed in the specification. Thus, the claimed method is not the method disclosed in the specification.

Claims 2-12 and 16-21 are included in this part of the rejection as dependent upon rejected claim.

Applicant traverses the rejection (Page 12 of Response of 28 November 2007, 3rd paragraph). The reasons for the traversal are:

"Even if the PBMCs are further stimulated, they are still the PBMCs in the biological sample and their secretions are what is being measured before and after administration of a potential treatment which is administered *in vivo*".

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

The plain meaning of "measuring .....in a biological sample from a mammalian subject" is that the measurement be performed directly on the sample obtained from the mammal. The method of the instant invention comprises obtaining a biological sample before and after treatment, stimulating PBMCs isolated from said biological sample in an *in vitro* system, and measuring cytokines secreted into the culture medium. Thus, the methods of the instant invention comprise treatment of subject, and determining cytokine secretion in an *in vitro* system. Applicant has omitted an essential step in the method: that of isolating PBMCs, stimulating said PBMCs in an *in vitro* culture system, and measurement of cytokines isolated from said culture system. Thus, the rejection is maintained.

Claim 22 remains rejected under 35 U.S.C. 112, 2nd paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant traverses the rejection (page 16, Response of 28 November 2007, 1st-3rd paragraph). The reason for the traversal is: claim 22 does specify two elements: a first measuring element or system for measuring the level of at least one anti-inflammatory cytokine and a second measuring element or system for measuring the level of at least one pro-inflammatory cytokine; furthermore, the claim does specify the interrelationship between the two measuring elements or systems.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

The elements or systems recited in the claims do not recite any structural limitations or concrete elements; rather they recite unspecified systems for performing steps in the method of the claimed invention. Additionally, the interrelationship between

the two systems comprises a computational step, determination of a ratio, and not a recitation of how the two components are related.

Claim 23 is included in this part of the rejection as dependent upon a rejected claim.

35 U.S.C. § 112, First Paragraph:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of Claim(s) 1-12 and 16-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement **(scope of enablement rejection)** is maintained for reasons of record and for reasons set forth below.

The specification is enabling for a method of determining the efficacy of a treatment of inflammatory diseases of the bowel in mammals *in vivo*:

a. wherein the cytokine levels are measured before and after treatment in a biological sample wherein the biological sample comprises a biopsy sample from the bowel, peripheral blood mononuclear cells that have been stimulated in vitro, gut lymphoid tissues with *in vitro* stimulation or gut lymphoid tissues without *in vitro* stimulation

b. wherein a treatment comprises administration of a treatment and/or a composition other than direct administration of anti-inflammatory cytokines or compositions which directly inhibit cytokines

c. wherein the changes in the ratios following administration of treatment which are indicative of efficacy of treatment (for inflammatory diseases of the bowel) are changes in the ratio of the level of IL-10 to the level of IL-12, changes in the ratio of level of TGF-beta to level of IL-12 or changes in the ratio of level of IL-10 to the level of IFN-gamma disease

However, the specification does not provide enablement for the full scope of the claims.

Applicant traverses the rejection (page 18, Response of 28 November 2007, last paragraph, bridging page 19, 2nd paragraph). The reasons for the traversal are:

1. Methods beyond those specified above (section a) are enabled because the "The Cytokine Handbook (pages 1384-1386) teaches "that measurement of plasma levels of cytokine are often not meaningful except in conditions associated with chronic cytokine release. "Thus, if IBS results in chronic, altered cytokine ratios, IBS may be a condition associated with chronic cytokine release and may be studied with methods of measuring cytokine levels in tissues other than those directly from the bowel region".

2. Applicant asserts that even though treatments involving administration of anti-inflammatory cytokines or compositions which interact directly with pro-inflammatory may be known, the methods of the application can be used to study the subject's response to the treatment and to determine the efficacy of the treatment.

3. Cytokine profiles are known, and levels of multiplex assay kits can measure multiple cytokines in a single sample. One of skill in the art would understand that other pro and anti-inflammatory cytokines could be used and studied.

Applicant's arguments have been fully considered but are not found to be persuasive for reasons of record and for reasons set forth below:

In response to 1: Applicant has not taught that IBS results in chronic, altered cytokine levels. Thus, one cannot determine if IBS is a condition which may be studied with methods of measuring cytokine levels in tissues other than those directly from the bowel region. Vilcek teaches (2003."The Cytokine Handbook" Chapter 1, page 6, Table 1.1) cytokine production is transient and the action radius is usually short (typical action is autocrine or paracrine, not endocrine). Papadakis et al (2000. Ann Rev Med 51:289-298, cited in Office Action of 23 August 2006) teach measurement of changes in cytokine profiles in inflamed intestinal mucosa in Crohn's disease and ulcerative colitis

(page 290, 3rd complete paragraph). Thus, while changes in cytokine profiles may be evident locally (gut region) in patients suffering from Crohn's disease or ulcerative colitis (IBDs), one could not predict that one would be able to detect changes in cytokine profiles in such biological samples as urine, plasma, serum, saliva, tissue biopsies, cerebrospinal fluid, since cytokines are known to be transiently expressed and act locally. It is noted that Table 1.2 indicates there are many exceptions to the autocrine or paracrine mode of action, but does not indicate that IBS is one of these exceptions. Thus, the specification merely presents the idea that cytokines may be measured in any "biological sample" [paragraph 0059 of PGPUB 20040228837, the PGPUB of the instant invention] and said resulting data would be useful in determining the efficacy of a treatment of inflammatory bowel disease. In view of the lack of further guidance in the specification, and the teachings in the art (see above discussion), this is an invitation to the skilled artisan to experiment to determine whether the measurement of cytokine levels in any given biological sample would present information useful in determining efficacy of treatment. Such an invitation to experiment is not enabling.

In response to 2: Administration of IL-10 or antibodies to pro-inflammatory cytokines are art-recognized methods of treating IBD. These treatments, by themselves, would result in increasing IL-10 levels and/or decreasing pro-inflammatory cytokine levels in biological samples drawn from the patient. These changes in cytokine levels would result in a change in the ratios of levels IL-10 to levels of IL-12 or levels of TNF-α or levels of IFN-γ, but one could not determine if these changes would be indicative of efficacy of treatment or are a result of administration of therapeutic compounds.

In response to 3: There is no question that one could measure multiple cytokines in any given assay, and use the results to calculate ratios. However, the claims are drawn to a method of determining efficacy of treatment by comparing ratios of levels of anti-inflammatory cytokine to pro-inflammatory cytokine before administration of treatment to that following administration of treatment. Therefore, one would first need

to determine a nexus between the unspecified cytokines and inflammatory bowel disease, and determine which cytokine ratios are meaningful indicators of efficacy of treatment. The determination of which ratios are meaningful (and when) is an essential part of the invention, and as such, the invention is not enabled until it has been reduced to practice.

It would require undue experimentation on the part of the skilled artisan to determine which cytokine ratios, and the changes therein would be indicative of efficacy of treatment of inflammatory diseases of the bowel.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of Claim 22 under 35 U.S.C. 102(b) as being anticipated by Vignali (2000 Journal of Immunological Methods 243:243-255) is maintained for reasons of record and for reasons set forth below.

Applicant traverses the rejection (page 20 of Response of 28 November 2007, 5th paragraph, bridging page 21, 1st paragraph). The reasons for the traversal are:

a. Vignali does not disclose a kit; the reference teaches assay methods to measure multiple cytokine levels simultaneously

b. Viganli does not disclose providing instructions to users of a kit instructing user in determining desired useful ratios; said instructions are functionally to kit product

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

Claim 22, given its broadest reasonable interpretation, recites a product for measuring multiple cytokines in a biological sample from a mammalian subject. A reasonable interpretation of the claims could interpret a kit to comprise, for example,

antibodies to cytokines in a vial or test tube; Flowmetrix System would certainly comprise the various components in separate vials or tube, thereby meeting the definition of a kit.

Vignali teaches a FlowMetrix System of quantifying the concentration of a number of cytokines simultaneously in a 100 µl sample. This system can be used at any time point of a treatment protocol to measure pro- and anti-inflammatory cytokines. Once the cytokine concentrations are known, the ratios may easily be determined by dividing the concentrations of anti-inflammatory cytokines by the concentrations of pro-inflammatory cytokines. The skilled artisan may then draw conclusions by comparing ratios. As stated previously, case law teaches where the only difference between a prior art product (Multiplex system) and a claimed product (kit) is printed matter that is not functionally related to the product, the content of the printed matter will not distinguish the claimed product from the prior art. In re Ngai, 367 F.3d 1336, 1339, 70 USPQ2d 1862, 1864 (Fed. Cir. 2004). One of ordinary skill in the art would certainly know how to calculate ratios and be able to interpret ratios of cytokines obtained from samples before and after treatment.

35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of Claim 23 under 35 U.S.C. 103(a) as being unpatentable over Vignali (2000 Journal of Immunological Methods 243:243-255) is maintained for reasons of record and reasons set forth below.

Applicant traverses the rejection (page 22 of Response of 28 November 2007, 1st paragraph). The reasons for the traversal are:

a. Vignali does not disclose a kit for measuring cytokines in a biological sample

b. There is no motivation to add a means for collecting biological samples

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

In response to a, see above discussion.

In response to b: Vignali teaches (page 248, 2nd column, section 6) "We have also used the FlowMetrix™ assay to measure cytokine levels in an animal model for toxic shock syndrome……". One of ordinary skill in the art would recognize that one must have a means for obtaining biological sample from animal. Thus, one would have the means to obtain the biological sample available as a separate structure (i.e. syringe in laboratory or clinical setting) or one could include said means as part of the kit to measure cytokines, since the reference teaches measuring cytokines in a biological sample.

The recent Supreme Court decision (KSR, 82 USPQ2d at 1396) forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. Under KSR, it is now apparent "obvious to try" may be an appropriate test in many situations. Where there is motivation to solve a problem (in this case, a means for obtaining a biological sample) and there are a finite number of identified, predictable solutions (said means being available in a separate structure or package, or enclosed within the recited kit), a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation, but of ordinary skill and common sense. The fact that a combination was obvious to try might show that it was obvious under 103. *KSR Int'lCo. V. Teleflex Inc,*.127 S. Ct. 1727. 82 USPQ2d 1385, 1397 (2007).

The rejection of Claims 1-5, 9, 16, 17, 19, and 20 under 35 U.S.C. 103(a) as being unpatentable over Togawa et al. (2002 Am J. Physiol, Gastrointestinal Liver Physiol 283:G187-G195) is maintained for reasons of record and for reasons set forth below.

Applicant traverses the rejection (page 23 of Response of 28 November 2007, 1st paragraph). The reason for the traversal is: Togawa does not provide any suggestion to study "before and after" results or to set up such experiments.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

Togawa et al teaches evaluating the therapeutic effect of lactoferrin (treatment) in TNBS-administered rats starting from the day on which TNBS was administered (said administration induces experimental colitis) until death. Animals were divided into four groups; among the groups were TNBS-administered rats receiving 0.9% saline (IBS-control group) and TNBS-administered rats receiving lactoferrin as treatment (IBS-treated group) (page G188, 1st column, last paragraph). The reference teaches determination of pro-inflammatory and anti-inflammatory cytokines in various groups 7 days after TNBS administration (G188, 2nd column, 2nd complete paragraph) and teach "TNF-α and IL-β" concentrations (in colonic tissue) were significantly suppressed by the administration of lactoferrin" (page G191, 2nd column, 1st paragraph). Thus, contrary to Applicant's assertion, the reference compares cytokine levels in untreated TNBS rats to cytokine levels in TNBS rats treated with lactoferrin. While Togawa et al do not teach measuring the level of anti-inflammatory and pro-inflammatory cytokines before administering treatment, or determining the ratio of levels of anti-inflammatory cytokine to level of pro-inflammatory cytokine before and after treatment, it would have been obvious to the person of ordinary skill in the art at the time the invention was made, treating IBS patients, to measure cytokine levels in a biological sample before administration of treatment and after treatment to assess efficacy of treatment. A

person of ordinary skill in the art would have been motivated to make those modifications because Togawa et al teach "although it is not possible to extrapolate findings from animal models to the clinical situation, these data suggest that lactoferrin is potentially attractive as a therapeutic strategy for the treatment of inflammatory bowel disease" (page G194, 1st column, 1st paragraph), thus suggesting clinical experimentation to determine efficacy of the administration of lactoferrin. The skilled artisan, following the teaching of Togawa et al, would be motivated to measure cytokine levels before treatment in a clinical setting, instead of measuring levels in control animals, as the artisan would be aware of that such study design is standard protocols in clinical research. Furthermore, knowing the results of measurements of cytokine levels (as shown, for example, in Figure 5), one would be motivated to compute ratios as a way of determining shifts in patterns of cytokine levels. One would reasonably expect success because method of measuring cytokine levels in biological samples is well known in the art, and is taught by Togawa et al.

The rejection of Claims 18 and 21 under 35 U.S.C. 103(a) as being unpatentable over Togawa et al. as applied to claims 1, 17 and 20 in view of Vignali et al. (cited above and in previous Office Action) is maintained for reasons of record and for reasons set forth below.

Applicant traverses the rejection (page 24 of Response of 28 November 2007, 1st and 2nd complete paragraph). The reason for the traversal is: Neither Togawa nor Vignali teaches or suggests a clinical method using samples from a biological subject in which cytokine levels are determined and ratios analyzed.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

As stated above, Togawa et al suggest clinical experimentation to determine efficacy of the administration of lactoferrin. The clinical researcher would be motivated to measure cytokine levels before treatment in a clinical setting, instead of measuring levels in control animals as taught by Togawa et al, since such is standard practice in clinical research. Togawa et al teach measuring levels of at least one anti-inflammatory cytokine and at least one pro-inflammatory cytokine in a biological sample by ELISA using assay kits with the quantitative immunometric sandwich enzyme immunoassay technique. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of Togawa et al and substitute the multiplex assay taught by Vignali for the ELISA assay taught by Togawa et al. One would be motivated to make this substitution, and anticipate success since both assays involve immunological methods of measuring cytokine concentrations and Vignali teaches a more efficient method of quantifying the concentration of 15 cytokines simultaneously. As stated above, knowing the results of measurements of cytokine levels, one would be motivated to compute ratios as a way of determining shifts in patterns of cytokine levels.

The rejection of Claims 6-8 under 35 U.S.C. 103(a) as being unpatentable over Togawa et al. as applied to claim 1 in view of Blumberg et al. (1999. Current Opinion in Immunology 11:648-656) is maintained for reasons of record and for reasons set forth below.

Applicant traverses the rejection (page 25 of Response of 28 November 2007, 1st paragraph). The reason for the traversal is:

Togawa et al do not teach or suggest establishing or analyzing any ratios of cytokines. Blumberg also does not teach or suggest establishing or analyzing ratios to evaluate efficacy of treatments, but notes that there is likely an on-going balance between pro- and anti-inflammatory cytokines in relation to inflammation.

In response to traversal of teachings of Togawa et al, see discussion above.

Additionally, Togawa et al. teaches measurement of anti-inflammatory cytokines IL-4 and IL-10 and measurement of pro-inflammatory cytokines TNF-α, IL-1β and IL-6. The teachings of Blumberg et al are directed to inflammatory bowel disease, not any generic inflammatory condition, and note the importance of a balance of pro-inflammatory cytokines such as IFN-γ, TNF, and IL-12 and anti-inflammatory cytokines such as IL-10 and TGF-β. The reference teaches that IL-12 is a key factor in the pathogenesis of the TNBS-induced colitis model (the model taught by Togawa et al) and induces overproduction of IFN-γ and TNF. Blumberg et al also teach that mucosal inflammation can be viewed as a failure of production of suppressor cytokines such as TGF-β and IL-10. Thus, Blumberg et al teach the importance of the balance (ratio) between pro-inflammatory cytokines such as IFN-γ, TNF, and IL-12 and anti-inflammatory cytokines such as IL-10 and TGF-β. Both Togawa et al. and Blumberg et al. teach the importance of disturbed balance between proinflammatory and anti-inflammatory cytokines in inflammatory bowel disease. Thus, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of Togawa et al and substitute measurement of the pro-inflammatory cytokines taught by Blumberg et al (IFN-γ and IL-12) for the pro-inflammatory cytokine taught by Togawa et al (TNF-α, IL-1β and IL-6) and the anti-inflammatory cytokine taught by Blumberg et al (TGF-β) for the anti-inflammatory cytokine taught by Togawa et al (IL-10). One would be motivated to measure changes in cytokine levels, since Togawa et al teach changes in cytokine levels in response to therapeutic administration of lactoferrin. Once measurement of these cytokines is accomplished, the calculation of ratios would be obvious as a way of monitoring changes in the balance of levels of pro- to anti-inflammatory cytokines.

Conclusions:

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHULAMITH H. SHAFER whose telephone number is (571)272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao, Ph.D. can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lorraine Spector/, Ph.D.
Primary Examiner, Art Unit 1647

/Shulamith H. Shafer, Ph.D./
Examiner, Art Unit 1647